REMARKS

Upon entry of the present amendment, claims 54, 57-59, 61-69, 88-93, and 95-135 will be pending in the application. Claims 54, 58, and 61 have been amended. Claims 54 and 61 were amended to remove certain terms referring to a "portion," and claim 58 has been amended to read as an independent claim. No new matter has been added. As the present amendment places the application in condition for allowance or, at least, in better form for appeal, Applicant respectfully requests entry, even though a final Office action has been received.

Applicant and his representative appreciates Examiner Zeman's time and her comments made during a telephone interview with the undersigned on May 12, 2006 ("the telephone interview"). The substance of the interview is made of record in the remarks that follow.

35 U.S.C. § 112, ¶ 1

Claims 54, 57-59, 61-69, and 88-93 and 95-135 have been rejected as failing to comply with the enablement requirement (Office action at pages 2-8). In view of the present amendment and the remarks that follow, Applicant respectfully requests reconsideration and withdrawal of this ground for rejection.

The Examiner states (Office action at page 2; emphasis added):

> The specification, as originally filed, fails to provide an enabling disclosure for fusion proteins wherein the protein comprises an antigen (*or unidentified portion thereof*) or an influenza virus and a stress protein (*or unidentified portion thereof*) wherein the stress proteins (*or portions*) are selected from the list in claim 54. The specification only provides information for the stress proteins as names. *No specific sequences are identified* that the names refer to. ... One of skill in the art would require specific sequence information to make and use the invention of the claims.

As the emphasized passages indicate, the Examiner has considered, and rightly so, the significance of the inclusion of antigenic *portions* of an influenza antigen and *portions* of stress proteins in the fusion proteins now claimed. The Examiner is also concerned with "specific sequences" one can include in the claimed fusion proteins.

Independent claims 54 and 61 have been amended to remove the claim terms concerning "portions." This amendment was discussed during the telephone interview, and it is now made solely in the interest of advancing prosecution. As also discussed, the specific sequences of

influenza antigens and stress proteins recited in the present claims are known in the art, and such sequences were known at the time the present application was filed. As the claims no longer recite the terms concerning portions, and the sequences of influenza antigens and stress proteins were known in the art, one of ordinary skill in the art would have the sequences required.

Regarding the manner in which the claimed fusion proteins can be made, the Examiner states, "[t]here are an enormous number of polynucleotides, vectors, and host cells to be experimentally tested in order to make a useful polypeptide" as claimed (Office action at page 4). Clearly, by amending the claims to fusion proteins as shown above, and as discussed with the Examiner during the telephone interview, the amino acid sequences of the fusion proteins claimed, and therefore the sequences of polynucleotides encoding them, are much more limited. Moreover, Applicants' specification describes routinely practiced methods that can be used to construct any fusion protein within the scope of the claims and assays that demonstrate induction of an immune response.

As the amount of direction Applicants provide is an important consideration in assessing enablement, we now review some of the teaching set forth in the present specification. As noted above, amino acid sequences within the presently claimed fusion proteins were known in the art. In fact, Applicants stated this explicitly: "[s]tress genes and proteins for use in the present invention are those well known in the art" (specification at page 24, lines 3-4). They then go on to describe a number of suitable stress proteins (specification at pages 24-27). The methods for making fusion proteins were also well known, and Applicants not only referred to those methods but incorporated standard laboratory manuals describing them into the specification. Applicants state (specification at page 32, lines 13-23):

> The construction of expression vectors and the transfer of vectors and nucleic acids into various host cells can be accomplished using genetic engineering techniques, as described in manuals like *Molecular Cloning* and *Current Protocols in Molecular Biology*, which are hereby incorporated by reference, or by using commercially available kits (Sambrook, J., *et al.*, *Molecular Cloning*, Cold Spring Harbor Press, 1989; Ausubel, F.M., *et al.*, *Current Protocols in Molecular Biology*, Greene Publishing Associates and Wiley-Interscience, 1989)).

As noted in Applicants' prior Reply, and reiterated here as further evidence that those of ordinary skill in the art routinely made fusion proteins at the time the present application was filed,

Applicants' representative searched the PubMed database available through the National Center for Biotechnology Information (NCBI; www.ncbi.nlm.nih.gov) with the words "fusion" and "protein". Almost 100,000 papers were found, and about 30,000 of those papers were published before 1996. While some of these are bound to be irrelevant for the present purpose, the sheer volume of the publications in the field indicates the prevalence of fusion proteins and the familiarity those of skill in the art must have with them. It is well established and has been recognized on the record that the specification need not disclose what is well known to those of ordinary skill in the art (Prior Office action at page 3, citing the MPEP at 2164.05(a), 6th paragraph).

Applicants' working examples add significantly to the specification. Applicants have reviewed these examples on the record (see the Reply of December 16, 2005). The criticism of these examples is that "specific antigenic *portions* of those proteins [*i.e.*, the specific influenza antigens named in the claims] are not specifically disclosed" (Office action at page 7; emphasis added). Similarly, the specification is criticized for failing to disclose specific portions of stress proteins (Office action at page 7). These criticisms are no longer relevant to the presently claimed subject matter, as the terms relating to portions have been deleted from the claims.

There is no reason why one of ordinary skill in the art could not use Applicants' exemplary methods, or any others that were known in the art, to make any given fusion protein within the scope of the present claims. The same is true in evaluating an immune response in a mammal to whom a given fusion protein had been administered. These are routine methods, well within the abilities of those of ordinary skill in the art. The test for undue experimentation is not merely quantitative. A considerable amount of experimentation is permissible if it is merely routine or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. MPEP at 2164.06 citing *In re Wands*, 858 F.2d 731 (Fed. Cir. 1988) (citing *In re Angstadt*, 537 F.2d 489 (CCPA 1976)).

As in the prior Office action, one factor -- the quantity of experimentation necessary -- consumes the majority of the Examiner's statements. Here (and with language very similar to that used previously), the Examiner states:

> [t]here are an enormous number of polynucleotides, vectors, and host cells to be experimentally tested in order to make a useful polypeptide of a fusion protein comprising one of 7 influenza proteins (or unidentified portions thereof) in fusion with the at least 17 named stress proteins (or unidentified portions thereof) (Office action at page 4).

In view of the present amendment and the information Applicants previously presented regarding the quantity of experimentation required, Applicants respectfully request reconsideration. One of ordinary skill in the art would not have to, for example, use non-naturally occurring polynucleotide sequences at all to practice the full scope of the present invention. The specification sets out, and the amended claims now require, specific antigens of not only the influenza virus, but also specific stress proteins. The sequences of these components of the claimed fusion proteins were known in the art; they were (and are) readily available.

The existence of U.S. Patent No. 5,082,767 (herein, "Hatfield") is not enough to tip the balance of factors toward a finding of non-enablement, particularly given the present amendment. Even if there were reason to believe that Hatfield's teaching were relevant to the present invention, it would have been available (Hatfield issued long before the instant application was filed. The Examiner states, "Hatfield et al. is a single disclosure and as such is not a well known practice for enabling the instant invention, and thus not available to applicant on this basis." (Office action at page 6). It is true that Hatfield is not referred to often. As noted on the record, when recently checked, the U.S. Patent and Trademark Office's website contained 1,936 patents that include the term "fusion protein" in the claims. Nowhere (in no searchable field) did *any* of these patents include the term "codon pair utilization" or "codon pair" or "codon utilization" or "5,082,767" (Hatfield's patent number). But that does not negate the fact that Hatfield is a part of the prior art. Should one of ordinary skill in the art experience difficulty in producing a fusion protein under the conditions Hatfield studied, one could have easily found and relied on Hatfield to address the problems of that condition.

Making fusion proteins is unquestionably routine, and any fusion made can be readily tested in the assay provided in the specification. The nature of the invention is quite straightforward. Applicants have invented a fusion protein that includes one of each of the two components specified, by name (*e.g.*, nucleoprotein and an Hsp100-200), in their claims. Although molecular biology techniques may be required to produce these fusion proteins, the techniques are surely among the most frequently practiced, best understood, and reliable. Nothing on the record, including Hatfield, establishes that one of ordinary skill in the art would be forced to resort to undue experimentation to make and use the fusion proteins now claimed. The state of the art is high, as is the level of skill of those within the practice. Applicants' specification discloses more than sufficient information, including working examples demonstrating success with two fusion proteins within the scope of the claims. There is no reason to expect that others could not do the same with the same or different fusion proteins. In view the present amendment and the present remarks, the final remaining ground for rejection should be withdrawn.

CONCLUDING REMARKS

Should the Examiner remain unpersuaded, the favor of a telephone call to the undersigned is requested before further action in the present application.

A Petition for Extension of Time and the required fee are enclosed. Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

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Lee Crews, Ph.D.
Reg. No. 43,567

Fish & Richardson P.C.
225 Franklin Street
Boston, MA 02110
Telephone: (617) 542-5070
Facsimile: (617) 542-8906
21421942.doc